

## WEST Search History

DATE: Tuesday, April 30, 2002

09/865,859

<u>Set Name</u> side by side	<u>Query</u>	<u>Hit Count</u>	<u>Set Name</u> result set
<i>DB=USPT; PLUR=YES; OP=ADJ</i>			
L1	troglitazone	234	L1
L2	L1 and angiogenesis	11	L2
L3	L2 and inhibition	11	L3
L4	L3 and tumor	10	L4
L5	L3 and cancer	7	L5
L6	L5 and inhibition	7	L6
L7	L4 and inhibition	10	L7
L8	L5 and inhibition	7	L8

END OF SEARCH HISTORY

Welcome to STN International! Enter x:x

LOGINID:sssptal202sxq

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

STN  
4/30/02  
09/865,853

\* \* \* \* \* Welcome to STN International \* \* \* \* \*

NEWS 1 Web Page URLs for STN Seminar Schedule - N. America  
NEWS 2 Jan 25 BLAST(R) searching in REGISTRY available in STN on the Web  
NEWS 3 Jan 29 FSTA has been reloaded and moves to weekly updates  
NEWS 4 Feb 01 DKILIT now produced by FIZ Karlsruhe and has a new update frequency  
NEWS 5 Feb 19 Access via Tymnet and SprintNet Eliminated Effective 3/31/02  
NEWS 6 Mar 08 Gene Names now available in BIOSIS  
NEWS 7 Mar 22 TOXLIT no longer available  
NEWS 8 Mar 22 TRCTHERMO no longer available  
NEWS 9 Mar 28 US Provisional Priorities searched with P in CA/CAPLUS and USPATFULL  
NEWS 10 Mar 28 LIPINSKI/CALC added for property searching in REGISTRY  
NEWS 11 Apr 02 PAPERCHEM no longer available on STN. Use PAPERCHEM2 instead.  
NEWS 12 Apr 08 "Ask CAS" for self-help around the clock  
NEWS 13 Apr 09 BEILSTEIN: Reload and Implementation of a New Subject Area  
NEWS 14 Apr 09 ZDB will be removed from STN  
NEWS 15 Apr 19 US Patent Applications available in IFICDB, IFIPAT, and IFIUDB  
NEWS 16 Apr 22 Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS  
NEWS 17 Apr 22 BIOSIS Gene Names now available in TOXCENTER  
NEWS 18 Apr 22 Federal Research in Progress (FEDRIP) now available  
  
NEWS EXPRESS February 1 CURRENT WINDOWS VERSION IS V6.0d,  
CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP),  
AND CURRENT DISCOVER FILE IS DATED 05 FEBRUARY 2002  
  
NEWS HOURS STN Operating Hours Plus Help Desk Availability  
NEWS INTER General Internet Information  
NEWS LOGIN Welcome Banner and News Items  
NEWS PHONE Direct Dial and Telecommunication Network Access to STN  
NEWS WWW CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

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\* \* \* \* \* STN Columbus \* \* \* \* \*

FILE 'HOME' ENTERED AT 14:23:22 ON 30 APR 2002

=> file registry  
COST IN U.S. DOLLARS  
  
FULL ESTIMATED COST

SINCE FILE	TOTAL
ENTRY	SESSION
0.21	0.21

FILE 'REGISTRY' ENTERED AT 14:23:41 ON 30 APR 2002  
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.  
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COPYRIGHT (C) 2002 American Chemical Society (ACS)

STRUCTURE FILE UPDATES: 29 APR 2002 HIGHEST RN 409058-68-0  
DICTIONARY FILE UPDATES: 29 APR 2002 HIGHEST RN 409058-68-0

TSCA INFORMATION NOW CURRENT THROUGH July 7, 2001

Please note that search-term pricing does apply when  
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES  
for more information. See STNote 27, Searching Properties in the CAS  
Registry File, for complete details:  
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

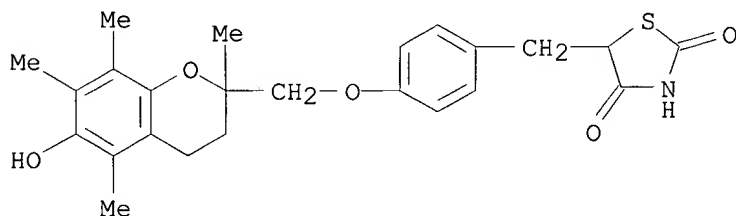
=> s troglitazone  
L1 9 TROGLITAZONE

=> d 11 1-9

L1 ANSWER 1 OF 9 REGISTRY COPYRIGHT 2002 ACS  
RN 343978-29-0 REGISTRY  
CN 2,4-Thiazolidinedione, 5-[[4-[(3,4-dihydro-6-hydroxy-2,5,7,8-tetramethyl-  
2H-1-benzopyran-2-yl)methoxy]phenyl)methyl]-, dihydrate (9CI) (CA INDEX  
NAME)

OTHER NAMES:

CN **Troglitazone dihydrate**  
MF C24 H27 N O5 S . 2 H2 O  
SR CA  
LC STN Files: CA, CAPLUS  
CRN (97322-87-7)



● 2 H2O

1 REFERENCES IN FILE CA (1967 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L1 ANSWER 2 OF 9 REGISTRY COPYRIGHT 2002 ACS  
RN 189764-85-0 REGISTRY  
CN 2,4-Thiazolidinedione, 5-[[4-[[ (2R)-3,4-dihydro-6-hydroxy-2,5,7,8-  
tetramethyl-2H-1-benzopyran-2-yl)methoxy]phenyl)methyl]-, (5S)- (9CI) (CA  
INDEX NAME)

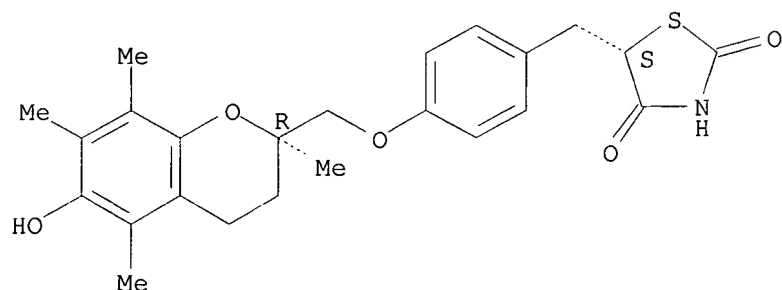
OTHER CA INDEX NAMES:

CN 2,4-Thiazolidinedione, 5-[[4-[(3,4-dihydro-6-hydroxy-2,5,7,8-tetramethyl-  
2H-1-benzopyran-2-yl)methoxy]phenyl)methyl]-, [S-(R\*,S\*)]-

OTHER NAMES:

CN **(2R,5S)-Troglitazone**  
 FS STEREOSEARCH  
 MF C24 H27 N O5 S  
 SR CA  
 LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

6 REFERENCES IN FILE CA (1967 TO DATE)  
 6 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L1 ANSWER 3 OF 9 REGISTRY COPYRIGHT 2002 ACS  
 RN 189764-84-9 REGISTRY  
 CN 2,4-Thiazolidinedione, 5-[[4-[(2S)-3,4-dihydro-6-hydroxy-2,5,7,8-tetramethyl-2H-1-benzopyran-2-yl]methoxy]phenyl]methyl]-, (5S)- (9CI) (CA INDEX NAME)

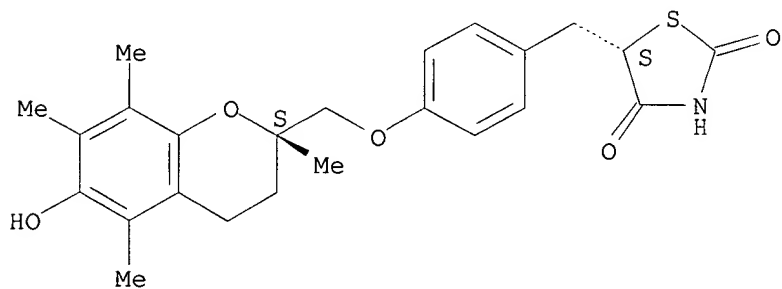
OTHER CA INDEX NAMES:

CN 2,4-Thiazolidinedione, 5-[[4-[(3,4-dihydro-6-hydroxy-2,5,7,8-tetramethyl-2H-1-benzopyran-2-yl)methoxy]phenyl]methyl]-, [S-(R\*,R\*)]-

OTHER NAMES:

CN **(2S,5S)-Troglitazone**  
 FS STEREOSEARCH  
 MF C24 H27 N O5 S  
 SR CA  
 LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.



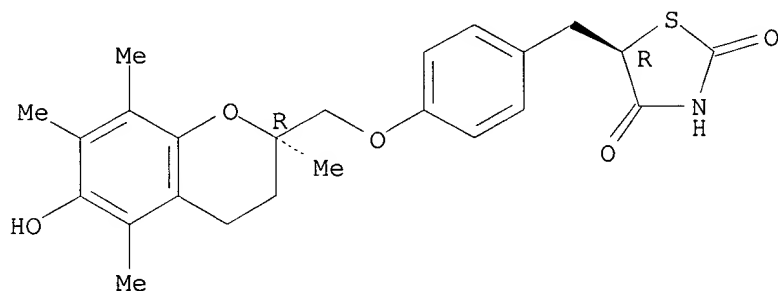
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

5 REFERENCES IN FILE CA (1967 TO DATE)  
 5 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L1 ANSWER 4 OF 9 REGISTRY COPYRIGHT 2002 ACS

RN 189764-83-8 REGISTRY  
 CN 2,4-Thiazolidinedione, 5-[[4-[[ (2R)-3,4-dihydro-6-hydroxy-2,5,7,8-tetramethyl-2H-1-benzopyran-2-yl]methoxy]phenyl]methyl]-, (5R)- (9CI) (CA INDEX NAME)  
 OTHER CA INDEX NAMES:  
 CN 2,4-Thiazolidinedione, 5-[[4-[[ (3,4-dihydro-6-hydroxy-2,5,7,8-tetramethyl-2H-1-benzopyran-2-yl)methoxy]phenyl]methyl]-, [R-(R\*,R\*)]-  
 OTHER NAMES:  
 CN **(2R,5R)-Troglitazone**  
 FS STEREOSEARCH  
 MF C24 H27 N O5 S  
 SR CA  
 LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.

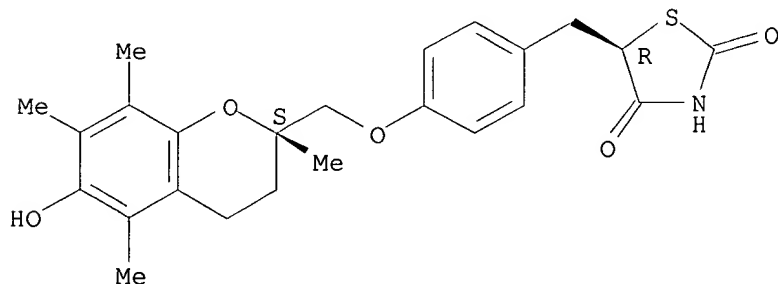


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

5 REFERENCES IN FILE CA (1967 TO DATE)  
 5 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L1 ANSWER 5 OF 9 REGISTRY COPYRIGHT 2002 ACS  
 RN 189764-81-6 REGISTRY  
 CN 2,4-Thiazolidinedione, 5-[[4-[[ (2S)-3,4-dihydro-6-hydroxy-2,5,7,8-tetramethyl-2H-1-benzopyran-2-yl]methoxy]phenyl]methyl]-, (5R)- (9CI) (CA INDEX NAME)  
 OTHER CA INDEX NAMES:  
 CN 2,4-Thiazolidinedione, 5-[[4-[[ (3,4-dihydro-6-hydroxy-2,5,7,8-tetramethyl-2H-1-benzopyran-2-yl)methoxy]phenyl]methyl]-, [R-(R\*,S\*)]-  
 OTHER NAMES:  
 CN **(2S,5R)-Troglitazone**  
 FS STEREOSEARCH  
 MF C24 H27 N O5 S  
 SR CA  
 LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.

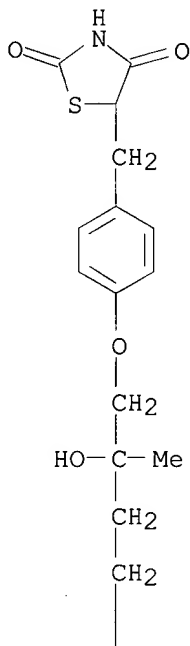


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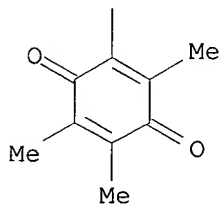
5 REFERENCES IN FILE CA (1967 TO DATE)  
5 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L1 ANSWER 6 OF 9 REGISTRY COPYRIGHT 2002 ACS  
RN 136665-44-6 REGISTRY  
CN 2,4-Thiazolidinedione, 5-[[4-[2-hydroxy-2-methyl-4-(2,4,5-trimethyl-3,6-dioxo-1,4-cyclohexadien-1-yl)butoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)  
OTHER NAMES:  
CN ROY 1358  
CN **Troglitazone quinone**  
FS 3D CONCORD  
MF C24 H27 N O6 S  
SR CA  
LC STN Files: BIOSIS, CA, CAPLUS, TOXCENTER, USPATFULL

PAGE 1-A



PAGE 2-A



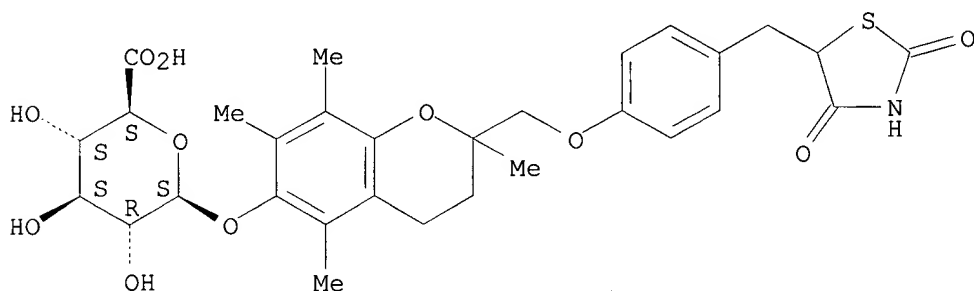
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

15 REFERENCES IN FILE CA (1967 TO DATE)

15 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L1 ANSWER 7 OF 9 REGISTRY COPYRIGHT 2002 ACS  
 RN 127040-01-1 REGISTRY  
 CN .beta.-D-Glucopyranosiduronic acid, 2-[[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenoxy]methyl]-3,4-dihydro-2,5,7,8-tetramethyl-2H-1-benzopyran-6-yl (9CI) (CA INDEX NAME)  
 OTHER NAMES:  
 CN ROY 1515  
 CN **Troglitazone glucuronide**  
 FS STEREOSEARCH  
 MF C30 H35 N O11 S  
 SR CA  
 LC STN Files: BEILSTEIN\*, CA, CAPLUS, TOXCENTER  
 (\*File contains numerically searchable property data)

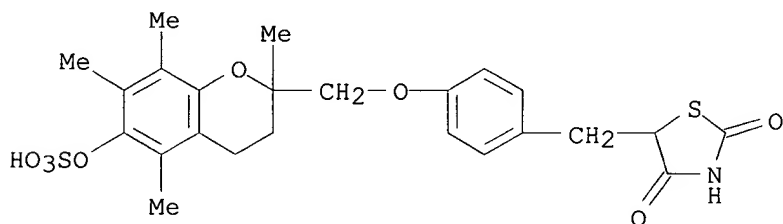
Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

10 REFERENCES IN FILE CA (1967 TO DATE)  
 10 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L1 ANSWER 8 OF 9 REGISTRY COPYRIGHT 2002 ACS  
 RN 107187-86-0 REGISTRY  
 CN 2,4-Thiazolidinedione, 5-[[4-[[3,4-dihydro-2,5,7,8-tetramethyl-6-(sulfooxy)-2H-1-benzopyran-2-yl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)  
 OTHER NAMES:  
 CN ROY 1357  
 CN **Troglitazone sulfate**  
 CN **Troglitazone sulfate ester**  
 FS 3D CONCORD  
 MF C24 H27 N O8 S2  
 CI COM  
 SR CA  
 LC STN Files: BIOSIS, CA, CAPLUS, TOXCENTER, USPATFULL



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

21 REFERENCES IN FILE CA (1967 TO DATE)  
21 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L1 ANSWER 9 OF 9 REGISTRY COPYRIGHT 2002 ACS  
RN 97322-87-7 REGISTRY  
CN 2,4-Thiazolidinedione, 5-[[4-[(3,4-dihydro-6-hydroxy-2,5,7,8-tetramethyl-2H-1-benzopyran-2-yl)methoxy]phenyl)methyl]- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 58: PN: WO0148150 SEQID: 73 claimed sequence

CN CI 991

CN CS 045

CN GR 92132X

CN Noscal

CN Rezulin

CN Romglizone

CN **Troglitazone**

FS 3D CONCORD

DR 259223-65-9

MF C24 H27 N O5 S

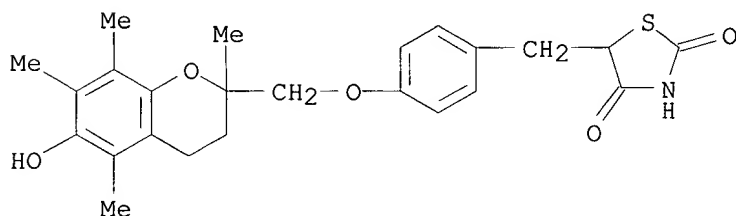
CI COM

SR CA

LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN\*,  
BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB,  
CEN, CHEMCATS, CIN, CSCHEM, DDFU, DIOGENES, DRUGNL, DRUGPAT, DRUGU,  
DRUGUPDATES, EMBASE, IPA, MEDLINE, MRCK\*, PHAR, PROMT, RTECS\*,  
SYNTHLINE, TOXCENTER, USAN, USPATFULL

(\*File contains numerically searchable property data)

Other Sources: WHO



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

786 REFERENCES IN FILE CA (1967 TO DATE)  
7 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
792 REFERENCES IN FILE CAPLUS (1967 TO DATE)

=> file caplus

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

18.60

18.81

FILE 'CAPLUS' ENTERED AT 14:24:32 ON 30 APR 2002

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FILE COVERS 1907 - 30 Apr 2002 VOL 136 ISS 18  
FILE LAST UPDATED: 29 Apr 2002 (20020429/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

=> s l1  
L2 795 L1

=> d his

(FILE 'HOME' ENTERED AT 14:23:22 ON 30 APR 2002)

FILE 'REGISTRY' ENTERED AT 14:23:41 ON 30 APR 2002  
L1 9 S TROGLITAZONE

FILE 'CAPLUS' ENTERED AT 14:24:32 ON 30 APR 2002  
L2 795 S L1

=> s l2 and angiogenesis  
12822 ANGIOGENESIS  
L3 10 L2 AND ANGIOGENESIS

=> d 1-10 ibib hitstr abs

L3 ANSWER 1 OF 10 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 2002:142506 CAPLUS  
DOCUMENT NUMBER: 136:177977  
TITLE: Methods for treating inflammatory diseases using PPAR agonists  
INVENTOR(S): Pershadsingh, Harrihar A.  
PATENT ASSIGNEE(S): USA  
SOURCE: PCT Int. Appl., 42 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 2  
PATENT INFORMATION:

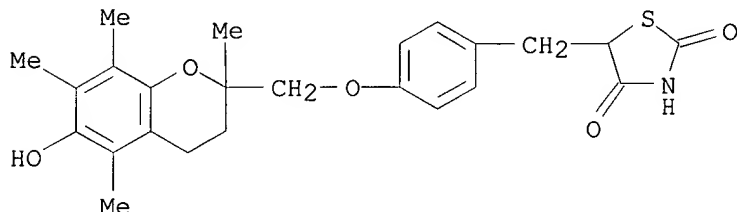
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002013812	A1	20020221	WO 2001-US25668	20010816
W: AU, CA, MX, NZ, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
PRIORITY APPLN. INFO.:				
			US 2000-225907P	P 20000817
			US 2000-230509P	P 20000906
IT 97322-87-7, Troglitazone				

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)

(methods for treating inflammatory diseases using PPAR agonists)

RN 97322-87-7 CAPLUS

CN 2,4-Thiazolidinedione, 5-[[4-[(3,4-dihydro-6-hydroxy-2,5,7,8-tetramethyl-  
2H-1-benzopyran-2-yl)methoxy]phenyl)methyl]- (9CI) (CA INDEX NAME)



AB The present invention describes methods for the use of PPAR ligands in the treatment inflammatory endocrine, dermatol., cardiovascular immunol., neurol., ophthalmic, neoplastic, pulmonary diseases, and age-related dysregulations. In addn., methods are provided for treating said conditions and diseases comprising the step of administering to a human or an animal in need thereof a therapeutic amt. of pharmacol. compns. comprising a pharmaceutically acceptable carrier, and a PPAR.gamma. agonist which cross-activates PPAR.alpha. or PPAR.delta. or both, or a PPAR.gamma. partial agonist, or a PPAR.gamma./RXR agonist, effective to reverse, slow, stop, or prevent the pathol. inflammatory or degenerative process.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:884254 CAPLUS

DOCUMENT NUMBER: 136:160858

TITLE: Top 200 medicines: can new actions be discovered through computer-aided prediction?

AUTHOR(S): Poroikov, V.; Akimov, D.; Shabelnikova, E.; Filimonov, D.

CORPORATE SOURCE: Institute of Biomedical Chemistry of the Russian Academy of Medical Sciences, Moscow, 119832, Russia

SOURCE: SAR and QSAR in Environmental Research (2001), 12(4), 327-344

CODEN: SQERED; ISSN: 1062-936X

PUBLISHER: Gordon & Breach Science Publishers

DOCUMENT TYPE: Journal

LANGUAGE: English

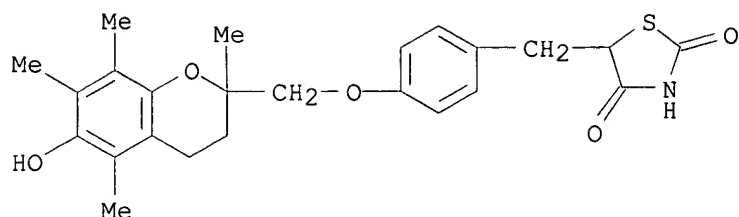
IT 97322-87-7, Troglitazone

RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(drug discovery through computer-aided prediction)

RN 97322-87-7 CAPLUS

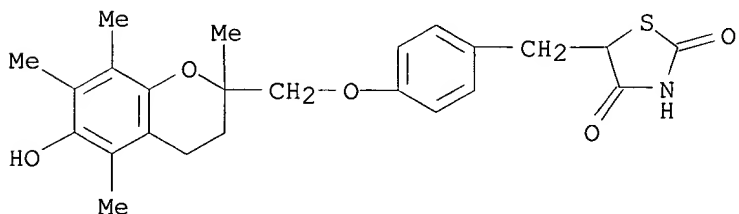
CN 2,4-Thiazolidinedione, 5-[[4-[(3,4-dihydro-6-hydroxy-2,5,7,8-tetramethyl-  
2H-1-benzopyran-2-yl)methoxy]phenyl)methyl]- (9CI) (CA INDEX NAME)



AB Computer-aided prediction of the biol. activity spectra by the program PASS was applied to a set of 130 pharmaceuticals from the list of the Top 200 medicines. The known pharmacol. effects were found in the predicted activity spectra in 93.2% of cases. Addnl., the probability of some supplementary effects was also predicted to be significant, including **angiogenesis** inhibition, bone formation stimulation, possible use in cognition disorders treatment, multiple sclerosis treatment, etc. These predictions, if confirmed exptl., may become a cause for a new application of pharmaceuticals from the Top 200 list. Most of known side and toxic effects were also predicted by PASS. PASS predictions at earlier R & D stages may thus provide a basis for finding new "leads" among already launched drugs and may help direct more attention to those particular effects of pharmaceuticals in clin. use which become apparent only in a small part of the population and require addnl. precautions.

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 2001:394831 CAPLUS  
 DOCUMENT NUMBER: 136:161068  
 TITLE: Response of experimental retinal neovascularization to thiazolidinediones  
 AUTHOR(S): Murata, Toshinori; Hata, Yasuaki; Ishibashi, Tatsuro; Kim, Sarah; Hsueh, Willa A.; Law, Ronald E.; Hinton, David R.  
 CORPORATE SOURCE: Department of Ophthalmology, Keck Sch. Med., University of Southern California, Los Angeles, CA, USA  
 SOURCE: Archives of Ophthalmology (Chicago, IL, United States) (2001), 119(5), 709-717  
 CODEN: AROPAW; ISSN: 0003-9950  
 PUBLISHER: American Medical Association  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 IT 97322-87-7, Troglitazone  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (response of retinal neovascularization to thiazolidinediones)  
 RN 97322-87-7 CAPLUS  
 CN 2,4-Thiazolidinedione, 5-[[4-[(3,4-dihydro-6-hydroxy-2,5,7,8-tetramethyl-2H-1-benzopyran-2-yl)methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)



AB To det. the effect of thiazolidinediones (TZDs) on exptl. retinal neovascularization. The ability of the TZDs troglitazone and rosiglitazone maleate (1-20 .mu.mol/L) to inhibit retinal endothelial cell (REC) proliferation, migration, tube formation, and signaling was detd. in response to vascular endothelial growth factor (VEGF). In vivo studies were performed using the oxygen-induced ischemia model of retinal neovascularization. Neonatal mice were treated with intravitreal injection of 0.5 .mu.L of troglitazone (100 .mu.mol/L) or rosiglitazone maleate (100 .mu.mol/L), or vehicle, and retinal neovascularization was assayed qual. and quant. by angiog. and histol. examn. Expression of the TZD receptor, peroxisome proliferator-activated receptor .gamma., was confirmed in RECs by Western immunoblotting. Rosiglitazone and troglitazone inhibited VEGF-induced migration, proliferation, and tube formation by RECs in vitro beginning at 10 .mu.mol/L. Rosiglitazone and troglitazone inhibited phosphorylation of extracellular signal-regulated mitogen-activated protein kinase 1 in RECs. Intravitreal injection of rosiglitazone or troglitazone inhibited development of retinal neovascularization but did not significantly inhibit VEGF overexpression in the ganglion cell layer of the ischemic retina. The TZDs inhibit exptl. retinal neovascularization with an effect that is primarily downstream of VEGF expression. The TZDs are widely prescribed and should be evaluated for their potential to inhibit the progression of diabetic retinopathy.

REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:337887 CAPLUS

DOCUMENT NUMBER: 135:132695

TITLE: Feedback control of arachidonate cascade in rheumatoid synoviocytes by 15-deoxy-.DELTA.12,14-prostaglandin J2

AUTHOR(S): Tsubouchi, Yasunori; Kawahito, Yutaka; Kohno, Masataka; Inoue, Ken-ichiro; Hla, Timothy; Sano, Hajime

CORPORATE SOURCE: First Department of Internal Medicine, Kyoto Prefectural University of Medicine, Kawaramachi-hirokoji, Kamigyo-ku, Kyoto, 602-8566, Japan

SOURCE: Biochemical and Biophysical Research Communications (2001), 283(4), 750-755  
CODEN: BBRC9; ISSN: 0006-291X

PUBLISHER: Academic Press

DOCUMENT TYPE: Journal

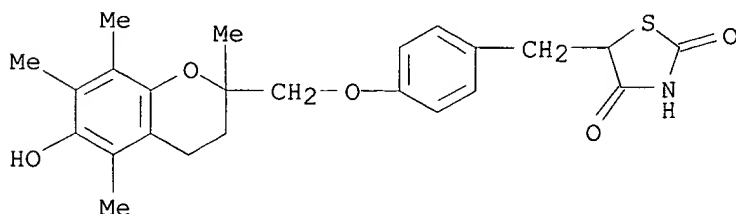
LANGUAGE: English

IT 97322-87-7, Troglitazone

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
(feedback control of arachidonate cascade in human rheumatoid synoviocytes by 15-deoxy-.DELTA.12,14-prostaglandin J2)

RN 97322-87-7 CAPLUS

CN 2,4-Thiazolidinedione, 5-[[4-[(3,4-dihydro-6-hydroxy-2,5,7,8-tetramethyl-2H-1-benzopyran-2-yl)methoxy]phenyl)methyl]- (9CI) (CA INDEX NAME)



AB Rheumatoid arthritis (RA) is a chronic polyarticular joint disease assocd. with massive synovial proliferation, inflammation, and **angiogenesis**. PPAR- $\gamma$ . ligands, both 15-deoxy- $\Delta^{12,14}$ -prostaglandin J2 (15d-PGJ2) and troglitazone (TRO), can inhibit the growth of RA synoviocytes in vitro, and suppress the chronic inflammation of adjuvant-induced arthritis in rats, but the potency of 15d-PGJ2 is higher than TRO. Prostaglandin (PG) E2 plays important roles in joint erosion and synovial inflammation. In the present study, 15d-PGJ2, but not TRO and other prostanoids, suppressed interleukin (IL)-1 $\beta$ -induced PGE2 synthesis in rheumatoid synovial fibroblasts (RSFs) through the inhibition of cyclooxygenase (COX-2) and cytosolic phospholipase A2 (cPLA2) expression. Furthermore, the inhibition was not affected by pretreatment with anti-PPAR- $\gamma$ . antibody. It means that this anti-inflammatory effect of 15d-PGJ2 for PG synthesis may be independent of PPAR- $\gamma$ . and 15d-PGJ2 is a key regulator of neg. feedback of the arachidonate cascade on the COX pathway. These findings provide new insight into the feedback mechanism of the arachidonate cascade. (c) 2001 Academic Press.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:259756 CAPLUS

DOCUMENT NUMBER: 134:361740

TITLE: Isoform-specific regulation of vascular endothelial growth factor (VEGF) family mRNA expression in cultured mouse brown adipocytes

AUTHOR(S): Asano, A.; Irie, Y.; Saito, M.

CORPORATE SOURCE: Graduate School of Veterinary Medicine, Department of Disease Control, Hokkaido University, Sapporo, 060-0818, Japan

SOURCE: Molecular and Cellular Endocrinology (2001), 174(1-2), 71-76

CODEN: MCEND6; ISSN: 0303-7207

PUBLISHER: Elsevier Science Ireland Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

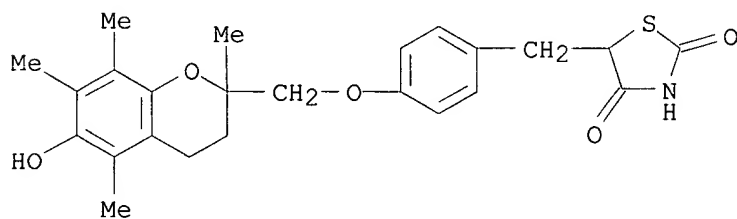
IT 97322-87-7, Troglitazone

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(PPAR- $\gamma$ . agonist; isoform-specific regulation of VEGF family mRNA expression in cultured mouse brown adipocytes)

RN 97322-87-7 CAPLUS

CN 2,4-Thiazolidinedione, 5-[[4-[(3,4-dihydro-6-hydroxy-2,5,7,8-tetramethyl-2H-1-benzopyran-2-yl)methoxy]phenyl)methyl]- (9CI) (CA INDEX NAME)



AB The authors have shown that brown adipose tissue (BAT), a thermogenic organ in mammals, expresses high levels of vascular endothelial growth factor (VEGF) mRNA in response to exposure to cold, which may contribute to **angiogenesis** assocd. with cold-induced hyperplasia of this tissue. In the present study, the authors examd. mRNA expression of not only VEGF, but also VEGF-B and VEGF-C, recently cloned VEGF isoforms, in

vitro using immortal brown adipocytes (HB2) isolated from mouse BAT. HB2 preadipocytes expressed detectable levels of VEGF, VEGF-B and VEGF-C mRNA, but a low level of VEGF. After HB2 cells differentiated into adipocytes, the VEGF mRNA level increased without a noticeable change in the VEGF-B and VEGF-C mRNA levels. When HB2 cells were stimulated by norepinephrine, the VEGF mRNA level increased without a change in that of VEGF-B, while the VEGF-C mRNA level decreased. A marked redn. of VEGF-C mRNA expression was also found when HB2 cells were treated with agonists of peroxisome proliferator-activated receptor .gamma. (PPAR.gamma., troglitazone), retinoic acid receptor (RAR, all-trans retinoic acid) and retinoid X receptor (RXR, 9-cis retinoic acid). These results suggest a specific adrenergic mechanism for up-regulation of VEGF expression different from those for other VEGF isoforms, and thereby the major contribution of VEGF to the cold-induced **angiogenesis** in BAT. In addn., the agonists of PPAR.gamma., RAR and RXR are suggested to be inhibitory to **angiogenesis** through the redn. of VEGF-C prodn.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:809642 CAPLUS

DOCUMENT NUMBER: 134:95235

TITLE: Remarkable tolerance of tumor cells to nutrient deprivation: possible new biochemical target for cancer therapy

AUTHOR(S): Izuishi, Kunihiro; Kato, Kazuyoshi; Ogura, Tsutomu; Kinoshita, Taira; Esumi, Hiroyasu

CORPORATE SOURCE: Investigative Treatment Division, National Cancer Center Research Institute, National Cancer Center Hospital East, Chiba, 277-8577, Japan

SOURCE: Cancer Research (2000), 60(21), 6201-6207  
CODEN: CNREA8; ISSN: 0008-5472

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

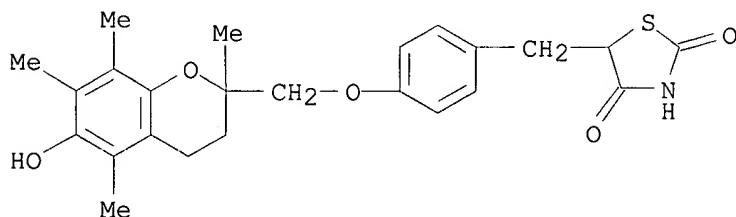
LANGUAGE: English

IT 97322-87-7, Troglitazone

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
(tolerance of tumor cells to nutrient deprivation response to)

RN 97322-87-7 CAPLUS

CN 2,4-Thiazolidinedione, 5-[[4-[(3,4-dihydro-6-hydroxy-2,5,7,8-tetramethyl-2H-1-benzopyran-2-yl)methoxy]phenyl)methyl]- (9CI) (CA INDEX NAME)



AB It was hypothesized that the tolerance to nutrient deprivation as well as **angiogenesis** might be an important factor for tumor progression under hypovascular conditions. When normal human fibroblasts were subjected to extreme nutrient starvation by culturing in a medium without serum, glucose, and amino acids, the cells died within 24 h. When liver cancer cell lines HepG2, Hep3B, HLE, and HuH-7 were tested, cell death occurred within 36 h. In contrast, four of six pancreas cancer cell lines (PANC-1, AsPC-1, BxPC-1, and KP-3) survived for markedly longer periods; >50% of the cells survived, even after starvation for 48 h. Of three

gastric cancer cell lines (MKN28, MKN45, and MKN74), only the most poorly differentiated (MKN45) cells survived >36 h. More than 50% of the cells in colon cancer cell lines SW480, WiDr, and DLD-1 survived >36 h, and the most undifferentiated (SW480) cell line survived longest. The possible involvement of protein kinase B (PKB)/Akt expression in the survival of various cell lines under nutrient starvation conditions was examd. High expression of PKB/Akt was assocd. with tolerance for nutrient starvation. When Akt antisense RNA expression vectors were introduced into PANC-1 cells, the tolerance was partially but significantly diminished by vectors for Akt1 and Akt2 but not Akt3. Because elimination of the tolerance might serve as a new strategy for cancer therapy, some compds. were tested for this purpose, and troglitazone, an insulin sensitizer, as well as LY294002, a phosphatidylinositol 3-kinase inhibitor, were found to kill PANC-1 cells only under conditions of nutrient starvation.

REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:368081 CAPLUS

DOCUMENT NUMBER: 133:12750

TITLE: Method using a PPAR.gamma. ligand/agonist for inhibiting **angiogenesis** and treating tumor growth

INVENTOR(S): Gerritsen, Mary E.; Xin, Xiaohua E.

PATENT ASSIGNEE(S): Genentech, Inc., USA

SOURCE: PCT Int. Appl., 52 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000030628	A2	20000602	WO 1999-US27612	19991118
WO 2000030628	A3	20011011		
W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
EP 1143953	A2	20011017	EP 1999-960538	19991118
EP 1143953	A3	20020206		
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			
US 2001036955	A1	20011101	US 2001-865859	20010525
PRIORITY APPLN. INFO.:			US 1998-109328P	P 19981120
			US 1999-116530P	P 19990120
			US 1999-443010	B1 19991117
			WO 1999-US27612	W 19991118

OTHER SOURCE(S): MARPAT 133:12750

IT 97322-87-7, Troglitazone

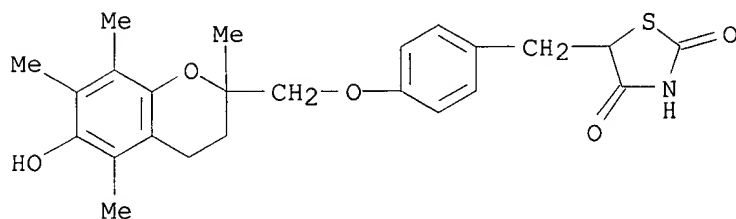
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(PPAR.gamma. ligand/agonist for inhibiting **angiogenesis** and treating tumor growth)

RN 97322-87-7 CAPLUS

CN 2,4-Thiazolidinedione, 5-[[4-[(3,4-dihydro-6-hydroxy-2,5,7,8-tetramethyl-

2H-1-benzopyran-2-yl)methoxy]phenyl)methyl]- (9CI) (CA INDEX NAME)



AB **Angiogenesis** is inhibited and the growth of tumors is treated by administering an effective amt. of a PPAR.gamma. ligand/agonist, optionally with an RXR receptor ligand.

L3 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:320014 CAPLUS

DOCUMENT NUMBER: 133:99344

TITLE: Peroxisome Proliferator-Activated Receptor-.gamma. Agonists Increase Vascular Endothelial Growth Factor Expression in Human Vascular Smooth Muscle Cells

AUTHOR(S): Yamakawa, Kenjiro; Hosoi, Masayuki; Koyama, Hidenori; Tanaka, Shinji; Fukumoto, Shinya; Morii, Hirotoshi; Nishizawa, Yoshiki

CORPORATE SOURCE: Second Department of Internal Medicine, Osaka City University Medical School, Osaka, 545-8586, Japan

SOURCE: Biochemical and Biophysical Research Communications (2000), 271(3), 571-574

CODEN: BBRCA9; ISSN: 0006-291X

PUBLISHER: Academic Press

DOCUMENT TYPE: Journal

LANGUAGE: English

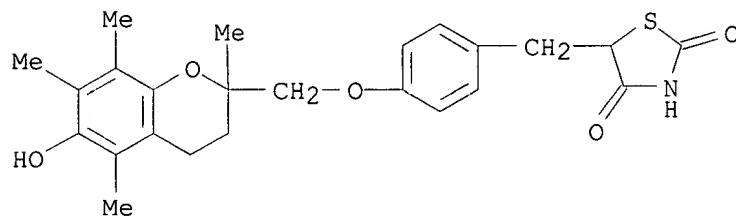
IT **97322-87-7**, Troglitazone

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(peroxisome proliferator-activated receptor-.gamma. agonists increase vascular endothelial growth factor expression in human vascular smooth muscle cells)

RN 97322-87-7 CAPLUS

CN 2,4-Thiazolidinedione, 5-[[4-[(3,4-dihydro-6-hydroxy-2,5,7,8-tetramethyl-2H-1-benzopyran-2-yl)methoxy]phenyl)methyl]- (9CI) (CA INDEX NAME)



AB Vascular endothelial growth factor (VEGF), expressed in a variety of mesenchymal cells including vascular smooth muscle cells (VSMC), is a potent mitogen for endothelial cells, and is used clin. applied for ischemic disease of peripheral vessels. To det. whether peroxisome proliferator-activated receptor .gamma. (PPAR.gamma.) regulates VEGF prodn. in VSMC, we examd. VEGF secretion from VSMC treated with PPAR agonists. Troglitazone increased VEGF secretion in a time- and



dose-dependent manner (261. $\pm$ .35% with 25 mM of troglitazone for 24 h), and also increased levels of VEGF mRNA. VEGF secretion was also increased by other PPAR. $\gamma$ . agonists, pioglitazone, LY171883, and 15d-PGJ2 (224. $\pm$ .17.1%, 247. $\pm$ .36.8% and 171. $\pm$ .7.8%, resp.), but not the PPAR. $\gamma$ . agonists bezafibrate and Wyl4643 (85.2. $\pm$ .1.5%, 94.6. $\pm$ .3.2, resp.). Our findings suggest that thiazolidinediones might be useful for the therapeutic **angiogenesis** for ischemic artery disease. (c)  
2000 Academic Press.

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 9 OF 10 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:15004 CAPLUS

DOCUMENT NUMBER: 132:73666

TITLE: Ophthalmic uses of PPAR- $\gamma$ . agonists and antagonists

INVENTOR(S): Pershadsingh, Harrihar A.; Levy, Daniel E.

PATENT ASSIGNEE(S): Photogenesis, Inc., USA

SOURCE: PCT Int. Appl., 43 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000000194	A1	20000106	WO 1999-US14262	19990625
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
AU 9947134	A1	20000117	AU 1999-47134	19990625
US 6316465	B1	20011113	US 1999-342381	19990628
PRIORITY APPLN. INFO.:			US 1998-90937P	P 19980627
			US 1998-90937	P 19980627
			WO 1999-US14262	W 19990625

OTHER SOURCE(S): MARPAT 132:73666

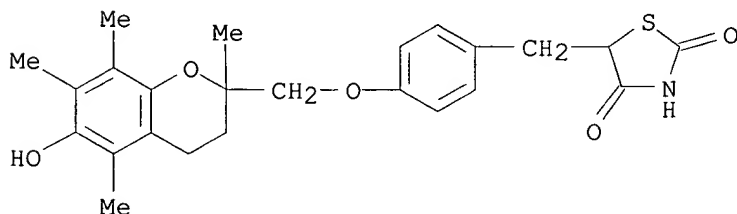
IT 97322-87-7, Troglitazone

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(ophthalmic uses of PPAR- $\gamma$ . agonists and antagonists)

RN 97322-87-7 CAPLUS

CN 2,4-Thiazolidinedione, 5-[[4-[(3,4-dihydro-6-hydroxy-2,5,7,8-tetramethyl-2H-1-benzopyran-2-yl)methoxy]phenyl)methyl]- (9CI) (CA INDEX NAME)



AB Methods are disclosed for treating diseases of ocular tissues expressing the nuclear receptor PPAR-.gamma., by inhibiting the inflammatory response, the neovascularization and **angiogenesis**, and programmed cell death (apoptosis) in these target tissues, comprising administering to a human or animal in need of treatment an effective amt. of a compd. that modifies the activity of PPAR-.gamma., or a pharmaceutically acceptable salt or solvate thereof. Novel compds. and methods for their synthesis are provided.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 10 OF 10 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:373898 CAPLUS

DOCUMENT NUMBER: 131:183259

TITLE: Angiogenic effect of lipid hydroperoxide on bovine aortic endothelial cells

AUTHOR(S): Yamada, Yasuyo; Nakanishi-Ueda, Takako; Yasuda, Masako; Armstrong, Donald; Yamamoto, Yorihiro; Yamamoto, Toshinori; Yasuhara, Hajime

CORPORATE SOURCE: Department of Pharmacology, School of Medicine, Showa University, Tokyo, 142-8555, Japan

SOURCE: Journal of Clinical Biochemistry and Nutrition (1998), 25(3), 121-130

CODEN: JCBNER; ISSN: 0912-0009

PUBLISHER: Institute of Applied Biochemistry

DOCUMENT TYPE: Journal

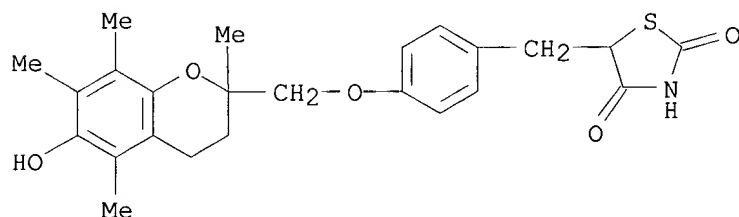
LANGUAGE: English

IT 97322-87-7, Troglitazone

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
(angiogenic effect of lipid hydroperoxide on bovine aortic endothelial cells)

RN 97322-87-7 CAPLUS

CN 2,4-Thiazolidinedione, 5-[[4-[(3,4-dihydro-6-hydroxy-2,5,7,8-tetramethyl-2H-1-benzopyran-2-yl)methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)



for 3 h was reduced from 5.1 pg/mg protein to 2.0 pg/mg protein by treatment with bucillamine. Apparently, 18:2-OOH induced BAEC growth is partly related to bFGF release or synthesis.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT